REMARKS

In the Office Action mailed January 12, 2005, Claims 1, 2, 5-17, 24-37, 39-66, 72-87, 94-107, and 109-133 were pending for consideration in the present application. All of such claims were rejected under 35 U.S.C. § 103(a) as allegedly obvious in view of one or more cited references. Specifically, Claims 1, 2, 5-17, 24-37, 39-47, 59-66, 72-87, 94-107, 109-114, and 126-133 were rejected in view of U.S. 5,589,513 (hereinafter "'513 Patent"), and Claims 1, 2, 5-8, 11, 24-27, 29-33, 36, 37, 39-59, 72-78, 81, 94-97, 99-103, 106, 107, and 109-126 were rejected in view of either U.S. 6,303,662 (hereinafter "'662 Patent") or GB 2098865 (hereinafter "'865 Patent").

Each of these rejections will be addressed in turn below. It is respectfully requested that the Examiner further consider the application in view of these remarks.

Rejections Under 35 U.S.C. § 103

The Examiner has rejected claims 1, 2, 5-17, 24-37, 39-66, 72-87, 94-107, and 109-133 as being unpatentable over the above-recited references. The Applicant respectfully submits that these claims are patentable over the cited reference for the reasons set forth below, and that the rejection should be withdrawn.

Before discussing the obviousness rejections herein, it is thought proper to briefly state what is required to sustain such a rejection. The issue under § 103 is whether the PTO has stated a case of *prima facie* obviousness. According to the MPEP § 2142, the Examiner has the burden and must establish a case of *prima facie* obviousness by showing the prior art reference, or references combined, teach or suggest all the claim limitations in the instant application. Further, the Examiner has to establish some motivation or suggestion to combine and/or modify the references, where the motivation must arise from the references themselves, or the knowledge generally available to one of ordinary skill in the art. The Applicant respectfully submits that the Examiner has not satisfied the requirement for establishing a case of *prima facie* obviousness in any of the rejections.

The Present Invention

The present invention as recited in independent Claim 1, provides for a pharmaceutical formulation having an active agent and a pharmaceutically acceptable vehicle. The active agent is found in two fractions, a solubilized fraction and a solid particle fraction. The solid particle fraction and the solubilized fraction are both present in the pharmaceutically acceptable vehicle. The presence of the active

ingredient in both a solubilized form and a solid form is an important element to the current invention.

Likewise, independent Claim 74 of the present application teaches a pharmaceutical system for the administration of an active agent, which also requires that the active agent be present in both a suspended or solid particulate phase and a solubilized phase.

Rejection in view of the '513 Patent

The Examiner has rejected claims 1, 2, 5-17, 24-37, 39-66, 72-87, 94-107, and 109-133 as allegedly obvious in view of U.S. '513. The U.S. '513 patent teaches pharmaceutical compositions comprising two phases and an MAO inhibitor as an active agent. The two phases of the composition are the "fast release" phase and the "slow release" phase and are specifically provided in order to allow long lasting MAO inhibition without producing certain adverse side effects. See, Col. 2, ln. 45-55.

To this end, in the embodiment disclosed for oral administration (i.e. an oral tablet) the active ingredient is located in both the fast and slow release phases of the composition and the active ingredient is in a solid form in both phases. See, Col. 6, ln. 40-55. In the embodiment disclosed for transdermal administration, a liquid crystal transdermal formulation is taught. In order to put the active agent into the liquid crystalline form, it is dissolved and suspended in a heated mixture of propylene glycol and Cremophor El. The heated mixture is mixed and additional ingredients are added and the mixture is allowed to cool. The final product is a composition in which 100% of the active agent is in a liquid crystalline state with an average particle size of from 8-10 microns. See, col. 7, ln.1-35. This transdermal formulation was then tested against control formulations with fewer liquid crystals of a much larger size. See, col. 11, ln. 1-46.

No other teachings of '513 patent teach or suggest that any of the drug be present in both a solubilized and particulate form in a single formulation. Therefore, neither the '513 reference by itself, nor as modified in any way suggested by the Examiner teaches or suggests all the elements of the present claims. Neither is there sufficient basis to provide one of ordinary skill in the art with adequate motivation to attempt to modify or combine the teachings of the '513 reference in order to arrive at Applicants' invention.

Accordingly, Applicants respectfully submit that the rejection of the claims in view of the '513 patent is improper and respectfully requested that it be withdrawn.

Rejection in view of the '662 and '865 Patents

The Examiner has also rejected claims 1, 2, 5-8, 11, 24-27, 29-33, 36, 37, 39-59, 72-78, 81, 94-97, 99-103, 106, 107, and 109-126 as allegedly unpatentable over the '662 and '865 patents.

The '662 patent teaches microemulsion compositions containing a highly polar and fat-soluble oil drug, a highly polar oil and a lowly polar oil. The preparation process starts when a "highly polar and fat-soluble drug is dissolved in the highly polar oil, mixed with the lowly polar oil and dissolved homogenously to give the oil phase" (Column 3, lines 64-67). The oil phase is combined with a fatty acid ester and a polyhydric alcohol and the resulting "gel" is diluted with water to form a microemulsion with small particles of the oil phase that contain the dissolved highly fat-soluble drug being emulsified in the water phase.

The importance of having the drug in a dissolved or solubilized state is shown in the col. 2, ln. 6. Here, the reference lists specific ranges with respect to the amounts of highly polar oil to the amount of fat-soluble drug, the ranges being 1-50 parts by weight of the oil to one part by weight of the drug, or preferably 1-20 parts by weight. The paragraph further states that "[i]n case of less than one part by weight, the highly polar and fat-soluble drug may be poorly dissolvable, while, in case of more than 50 parts by weight, the emulsion with minute particles may not easily obtainable." The clear stating of the ranges and their explained importance makes it clear that the drug in the cited reference is present in a dissolved state not in a solid particle state.

There is reference made in the specification of the '662 patent to the term "particle size" within the emulsion, however, the specification is clear that "particle size" refers to the size of the oil droplets in the emulsion and not to solid particles of drug present in the emulsion. Moreover, one of ordinary skill in the art would know that an emulsion does not contain solid particles *per se*.

The second cited reference, the '865 patent, teaches a microemulsion for delivering an active agent through the skin. The microemulsion includes an active agent, an emulsifier and co-emulsifier, and a fatty alcohol or mixture of water soluble and water-insoluble non-ionic surfactants.

In the Office Action the Examiner states that the '865 patent "teaches the same vehicles that are also described in the instant examples and specification, and accordingly ... it is the examiners position that the active agent prepared by the process of GB results in partially suspended and partially dissolved formulation." The applicant contends that this assumption is incorrect.

It is generally known to those skilled in the art that transdermal delivery of solid particles drugs is generally ineffective unless the drug is solubilized in a carrier. Thus, when developing a microemulsion specifically for transdermal delivery of "difficultly skin-penetrable pharmacologically active agents," it would be obvious to one skilled in the art to assure that these agents were fully solubilized so as to provide effective and efficient transdermal delivery. This is due to the generally known fact that drug that crystallizes into solid particles in the patch cannot be delivered through the skin. Therefore Applicants contend that one of ordinary skill in the art would not attempt to modify the teachings of the '865 patent in order to also include solid particles in the transdermal formulations.

Accordingly, Applicants respectfully submit that neither of the '662 or '865 patents teach or suggest each and every element of the present invention, either alone, in combination, or in any other modified form suggested by the Examiner. Moreover, Applicants submit that neither reference contains sufficient teachings or suggestions to motivate one of ordinary skill in the art to modify and apply such teachings in arriving at the present invention. Therefore, Applicants submit that the rejection of the present claims in view of the '662 and '865 patents is improper and respectfully request that it be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe that pending claims 1, 2, 5-17, 24-37, 39-66, 72-87, 94-107, and 109-133 present allowable subject matter and allowance thereof is respectfully requested. If any impediment to the allowance of these claims remains after consideration of the above remarks, and such impediment could be removed during a telephone interview, the Examiner is invited to telephone the undersigned attorney at (801) 566-6633 so that such issues may be resolved as expeditiously as possible.

Please charge any additional fees except for Issue Fee or credit any overpayment to Deposit Account No. 20-0100.

Dated this 12th day of May, 2005.

Respectfully submitted,

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